

REMARKS

Claims 49-61, 63-66, 68-70, and 72-75 are pending in the application. Claims 49, 68, and 69 have been amended to incorporate the limitations of claims 73-75. Claims 73-75 have been cancelled without prejudice. Claims 76-81 have been added. Support for the claims can be found throughout the specification. For example, support for new claims 76-78 can be found on page 7, lines 9-13 and Figures 3C and 6C. Support for new claims 79-81 can be found, for example, on page 16, lines 31-33. Following entry of the amendment, claims 49-61, 63-66, 68-70, 72, and 76-81 will be pending in the application.

Rejection of claims for obviousness under 35 U.S.C. §103(a)

I. Isner and Hammond

Claims 49-61, 63-66, and 68-75 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Isner, either PCT Patent Publication No. WO1997014307 or US Patent No. 6,121,246 ("Isner") in view of Hammond, US Patent No. 5,880,090 ("Hammond").

The rejection is respectfully traversed. The cited references, even in combination, fail to teach or suggest the features of the present invention in any manner sufficient to sustain the rejection.

In order to make out a *prima facie* showing of obviousness, the Examiner must establish that there is some motivation in one or the other of the cited references or in the state of the art at the time the invention was made to combine the references, the combination of references must teach or suggest each and every element of the claimed invention, and there must be some reasonable expectation of success in making and using the invention (M.P.E.P. §2143)..

Regarding the relationship between obviousness of a combination and the predictability of results, MPEP § 2143.01(III) states:

The mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art. *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385, 1396 (2007)("If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of

ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill.").

The issue of obviousness in chemical cases has been reviewed by the Courts in view of the recent KSR decision.

"While the KSR Court rejected a rigid application of the . . . TSM test in an obviousness inquiry, the Court acknowledged the importance of identifying 'a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does' in an obviousness determination."

"When there is a design need or market pressure to solve a problem and there is a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp." *KSR*, 127 S. Ct. at 1732. * * * That is not the case here. *Rather than identify predictable solutions for antidiabetic treatment, the prior art disclosed a broad selection of compounds any one of which could have been selected as a lead compound for further investigation.* Significantly, the closest prior art compound (compound b, the 6-methyl) exhibited negative properties that would have directed one of ordinary skill in the art away from that compound." *Takeda Chemical Industries Ltd. v. Alphapharm Pty.* 492 F.3d 1350 (Fed. Cir. 2007) [emphasis added]

The KSR decision does not abrogate the need for some suggestion in the reference or in the art to modify a particular reference in a particular manner.

The Office Action states that:

Isner (WO 97/14307) teaches a method for enhancing blood vessel formation or angiogenesis in an ischemic tissue in a mammal having cerebrovascular ischemia, renal ischemia, pulmonary ischemia, limb ischemia, ischemic cardiomyopathy and myocardial ischemia (page 4, lines 5-23). The method comprises *the step of injecting said tissue* with an effective amount of a nucleic acid capable of expressing an angiogenic protein by any injection means,.... Angiogenic protein includes aFGF, bFGF, VEGF (including VEGF165, see page 15, line 19), EGF, PDGF, PD-ECGF, HGF, colony stimulating factor (CSF), macrophage-CSF (mCSF), granulocyte/ macrophage-CSF (GM-CSF) and nitric oxidesynthase or muteins or portions thereof (page 5, lines 10-22). (page 3, underline in Office Action, further emphasis added by Applicant)

Therefore, per the teachings of Isner, and as noted in the Office Action:

1. Angiogenic proteins are injected into the ischemic tissue.

2. GM-CSF is an angiogenic protein.

Modification of Isner to inject an angiogenic protein to a site other than the ischemic tissue would be contrary to the teachings of the invention as noted in the prior response. Applicant cites the following teachings from Isner:

“nucleic acid... capable of expressing an angiogenic protein... ***when injected into an ischemic tissue*** induces angiogenesis, providing the ischemic tissue with increased blood vessels.” (page 4, lines 5-9)

“a method for treating ischemic tissue in a mammal which comprises ***injecting said tissue*** with an effective amount of a nucleic acid capable of expressing an angiogenic protein.” (page 4, lines 13-16)

“The ***ischemic tissue may be injected*** with the nucleic acid by any injection means.” (page 4, lines 25-26)

As noted in the prior response, this injection directly into ischemic tissue was to overcome the limitations of the prior art. It was not an arbitrary choice. ***Identification of GM-CSF by Isner as an angiogenic protein means that the protein would need to be administered to the ischemic tissue.*** The method of Isner could not be modified to include injection of GM-CSF to another site, e.g., systemically, as now claimed.

Having been provided with the teachings of Isner regarding past failures of systemic injection of angiogenic protein, ‘a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does’ cannot be provided by Hammond or any other reference. Isner defined GM-CSF as an angiogenic protein. No ‘reason that would have prompted a person of ordinary skill in the art’ to reclassify the GM-CSF otherwise has been provided, as would be necessary to combine the inventions to arrive at the instantly claimed invention. Further, Isner’s teaching that GM-CSF is an angiogenic protein would not suggest an advantage for its use with a second angiogenic protein.

Applicant has further added claims 76 to 78 in which the method results in an increase in neovascularization from 50% to 300% in the ischemic tissue; and claims 79 to 81 in which the GM-CSF is administered one week prior to treatment with the nucleic acid encoding at least one angiogenic protein or an effective fragment thereof into the myocardial tissue. Applicant

submits that there can be no reason to expect such a high level of neovascularization based on the combined teachings of Isner and Hammond, and that neither reference teaches or suggests the timing of administration of various factors. Applicant submits that claims 49-61, 63-66, 68-70, 72, and 76-81 are not obvious in view of the cited art. Withdrawal of the rejection is respectfully requested.

II. Isner and Bussolino

Claims 49-61, 63-66, 68-70 and 72 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over either Isner (WO 97/14307) or Isner (US Patent 6,121,246) in view of Bussolino.

The rejection is respectfully traversed. The cited references, even in combination, fail to teach or suggest the features of the present invention in any manner sufficient to sustain the rejection.

However, to progress the prosecution of the instant application, Applicant has amended independent claims 49, 68, and 69 to include the limitations of claims 73 to 75, respectively. As claims 73 to 75 are not included in the rejection, the rejection is overcome.

III. Isner, Bussolino, and Pierce

Claims 73-75 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over either Isner (WO 97/14307) or Isner (US Patent 6,121,246) in view of Bussolino further in view of Pierce.

The rejection is respectfully traversed. The cited references, even in combination, fail to teach or suggest the features of the present invention in any manner sufficient to sustain the rejection.

This combination of references fails for the same reason as the references set forth above. Isner teaches that angiogenic agents must be administered to ischemic tissue. Further, Isner teaches that GM-CSF is an angiogenic agent. *Isner cannot be modified to include administration of an angiogenic agent systemically, as now claimed, as Isner teaches that the*

failure of prior art methods was due to the administration of angiogenic agents systemically.

Applicant submits that claims 73-75 are not obvious in view of the cited art. Withdrawal of the rejection is respectfully requested.

In sum, there is nothing in any of the cited references or in the state of the art at the time the invention was made that provides one of ordinary skill in the art with the motivation to combine the references in the manner proffered by the Examiner. Accordingly, withdrawal of the rejection is respectfully requested.

Double Patenting Rejections

Claims 49-61, 63-66, 68-70, and 72-75 are provisionally rejected under the judicially created doctrine of double patenting over claims 1-15 of U.S. Patent No. 6,121,246 in view of Bussolino and Pierce.

Applicant respectfully requests that the provisional rejection be held in abeyance until allowable matter is incited in the instant application. Applicants will address the double patenting rejections of the claims upon a finding that the claims (that will be pending upon entry of the amendments and remarks presented herein) are in condition for allowance, but for the instant double patenting rejection. Filing of a terminal disclaimer will be considered at that time.

CONCLUSION

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of all rejections and allowance of the application with claims 49-61, 63-66, 68-72, and 76-81 presented herein. In advance of the issuance of a final Office Action, Applicants invite the Examiner to call the undersigned at the telephone number indicated below to schedule an interview.

Request for Extension of Time for Reply and Fee Authorization

Applicant requests a two month extension of time for reply to the Office Action. The Commissioner is hereby authorized to charge Deposit Account No. 04-1105, referencing Docket No. 47624DVC(71417) the amount for the fee for the extension of two months and for the three additional claims added in the instant amendment, large entity.

Applicants believe that no additional fee is due to consider the present amendment. Nevertheless, the Director is hereby authorized to charge or credit any deficiency in the fees filed, asserted to be filed, or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account referencing the Docket Number provided.

Request for Interview

To expedite the prosecution of this case, Applicant requests a telephonic interview with the Examiner prior to the review of the Office Action. Applicant will contact the Examiner to arrange an interview time agreeable to the Examiner closer to the time that the Examiner will consider the response herein.

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Respectfully submitted,

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